

# PATENT

Docket No. US DEAV2002/0058 US NP

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of  
Stroebe et al.

Examiner: Not Yet Assigned

Art Unit: Not Yet Assigned

Application No.: 10/636,001

Filed: August 7, 2003

Title: Acylated Arylcycloalkylamines and Their Use as  
Pharmaceuticals

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## INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. 1.56, 1.97 AND 1.98

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Sir:

Applicants submit herewith patents, publications, and other information of which they are aware, which they believe may be material, as defined in 37 C.F.R. 1.56(b), to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 C.F.R. 1.56(a). While the information referred to in this Information Disclosure Statement may be material pursuant to 37 C.F.R. 1.56(b), the filing of this Information Disclosure Statement is not intended to, pursuant to 37 C.F.R. 1.97(h), constitute an admission that any patent, publication or other information referred to is, or is considered to be, material to the patentability of this invention. Pursuant to 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information exists.

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- ☐ (b) This Information Disclosure Statement is filed after the period set forth in 37 C.F.R. 1.97(b), but is believed to be filed before the mailing date of a final action under §1.113 or a notice of allowance under §1.311, whichever occurs first.
- ☐ (1) The undersigned attorney certifies that each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement;
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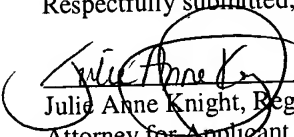
A concise explanation of the relevance of WIEHL, et al. as listed on the attached PTO-1449 (modified) is as follows:

**Asymmetric Reductive Amination of Cycloalkanones, 5<sup>1</sup> Synthesis and Absolute Configuration of 2-Substituted Cyclopentanamines**

In an asymmetric synthesis 2-substituted cyclopentanamines are obtained from racemic cyclopentanones by means of reductive amination in a three-step procedure. Condensation of the ketones **3(n)** with optically active 1-phenylethylamines yields imine mixtures **4(n)**, which are hydrogenated with Raney nickel to give the optically active, diastereomerically pure secondary amines **5(n)**. Hydrogenolysis with Palladium-on-charcoal leads to high grade enantiomerically pure primary amines **6(n)** with good yields. The relative configuration of the amines **5(n)** and **6(n)** is elucidated by <sup>1</sup>H and <sup>13</sup>C NMR techniques. The absolute configuration is determined by X-ray analysis of the 4-bromobenzamide **8** of the primary amine (+)-**6(n)** and with the help of CD of the salicylidene **9(n)**. The kinetically controlled asymmetric hydrogenation with a first order transformation as proved reaction mechanism in the cyclohexanamine line is confirmed for this investigation. The hydrogenation runs like-induced to the cis-configured amines **5(n)** and **6(n)**, respectively.

Respectfully submitted,

Date: September 30, 2003

  
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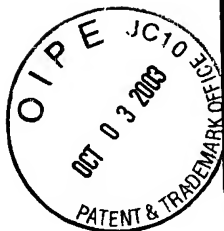
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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

**Compleat if Known**

<b>Application Number</b>	10/636,001
<b>Filing Date</b>	August 7, 2003
<b>First Named Inventor</b>	STROBEL, et al.
<b>Group Art Unit</b>	
<b>Examiner Name</b>	
<b>Attorney Docket Number</b>	DEAV2002/0058 - US - NP

Sheet	1	of	2
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Date	
Considered	

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 2

### Complete if Known

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Examiner Name	
Attorney Docket Number	DEAV2002/0058 - US - NP

### OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		AGGARWAL, et al., Catalytic Cyclopropanation Of Alkenes Using Diazo Compounds Generated In Situ. A Novel Route To 2-Arylcyclopropylamines, Org. Letters, 2001, 3 (17) 2785-2788	
		BROWN, et al., Organoboranes For Synthesis 7. An Improved General Synthesis of Primary Amines From Alkenes via Hydroboration-Organoborane Chemistry, Tetrahedron, 1987, 43 (18), 4071-4078	
		COUTTS, et al., Neurochemical and Neuropharmacological Properties of 4-Fluorotranlylcypromine, Cell. Mol. Neurobiol., 1987, 7 (3), 271-291	
		ENDRES, et al., Stroke Protection By 3-hydroxy-3-methylglutaryl (HMG)-CoA Reductase Inhibitors Mediated By Endothelial Nitric Oxide Synthase, Proc. Natl. Acad. Sci. USA, 1998, 95, 8880-8885	
		LI, et al., Activation Of Protein Kinase Ca and or e Enhances Transcription of the Human Endothelial Nitric Oxide Synthase Gene, Mol. Pharmacol., 1998, 53, 630-637	
		MOROI, et al., Interaction Of Genetic Deficiency Of Endothelial Nitric Oxide, Gender, and Pregnancy In Vascular Response To Injury In Mice, J. Clin. Invest., 1998, 101 (6), 1225-1232	
		NAKAYAMA, et al., T-786- C Mutation in the 5' -Flanking Region Of The Endothelial Nitric Oxide Synthase Gene Is Associated With Coronary Spasm, Circulation, 1999, 99, 2864-2870	
		SESSA, et al., Chronic Exercise In Dogs Increases Coronary Vascular Nitric Oxide Production And Endothelial Cell Nitric Oxide Synthase Gene Expression, Circ. Research, 1994, 74, 349-353	
		VARENNE, et al., Percutaneous Gene Therapy Using Recombinant Adenoviruses Encoding Human Herpes Simplex Virus Thymidine Kinase, Human PAI-1, and Human NOS3 in Balloon-Injured Porcine Coronary Arteries, Hum. Gene Ther. 2000, 11, 1329-1339	
		WIEHL, et al., Synthese Und Absolute Konfiguration 2-Substituierter Cyclopentanamine, Chem. Ber. 1986, 119, 2668-2677	

Examiner  
Signature

Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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